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AKTIP, A NEW LAMIN INTERACTING PROTEIN IS INVOLVED IN TELOMERE METABOLISM AND DNA REPLICATION

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Telomeres, replication, lamins

Proper telomere maintenance is a crucial process needed to protect the genome against instability and telomere dysfunction that has been linked to tumorigenesis and premature aging. Driven by results assigning a telomeric role to its *Drosophila* homologue *peo*, we have collected a set of data on a new human gene that can be linked to telomere metabolism, AKTIP. AKTIP down regulation triggers proliferation impairment, premature senescence and DNA damage response activation. AKTIP KD causes telomere dysfunction, as indicated by the presence of DNA damage foci at telomeres (TIFs) and by that of aberrant telomeres in AKTIP KD $p53^{-/-}$MEFs, including multiple telomeric signals at the ends of chromosomes, also known as fragile telomeres, indicative of telomere replication impairment. The mechanistic role of AKTIP appears, indeed, to be linked to replication: AKTIP can interact with DNA and with crucial components of the replisome (RPA and PCNA), furthermore, AKTIP KD cells display an intra-S block. A particularly seducing aspect of AKTIP comes from its localization, characterized by a typical punctate signal at the nuclear rim. This pattern is consistent with the interaction of AKTIP with nuclear lamins, which we have assessed by GST-pull down and mass spectrometry, and also with that with components of the replication forks (e.g. PCNA), which typically situate at the periphery of the nucleus in the final part of S-phase.

Taken together, our data suggest that AKTIP could become a new important player of the mechanistic scenarios of different human diseases linked to “telomeraging” including cancer and laminopathies.